antiinflammatories, antiparasitics, miotics, anticholinergics, adrenergics, antivirals, local anesthetics, antifungals, amoebicidals, trichomonocidals, analgesics, mydriatics, antiglaucoma drugs, carbonic anhydrase inhibitors, ophthalmic diagnostic agents, ophthalmic agents used as adjuvants in surgery, chelating agents, antineoplastics, antihypertensives, muscle relaxants, diagnostics, and mixtures thereof.

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**Remarks**

This is in response to the Examiner's communication mailed July 15, 2002. This response is being filed within TWO MONTHS of the mailing date of the final action; because September 15, 2002 fell on a Sunday, this response is being submitted on the next succeeding business day.

Claims 36-68 were pending. By way of this response, claim 42 has been canceled, and claims 36, 40, 41, 43-46, 48, 49, 51-53, 59, 60, 63, and 64 have been amended. Accordingly, claims 36-41, and 43-68 remain pending.

As a preliminary matter, applicant acknowledges that claims 40, 45, 49-58, 63, and 65-68 are free from the art and that these claims have only received a provisional obviousness-type double patenting rejection or have been rejected under 35 U.S.C. § 112, second paragraph. As discussed herein, applicant is willing to file a terminal disclaimer to address the provisional obviousness-type double patenting rejection upon the indication of otherwise allowable subject matter.

Items 1-2 of the Office Action - Rejections Under 35 U.S.C. § 112, second paragraph

Claims 36-68 remain rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention.

Regarding the statement that claims 48, 49, and 53 do not further limit the composition of claim 36, applicant respectfully disagrees and has amended claims 48, 49, and 53 to make the claims more clear as to how the composition of claim 36 is further limited. In particular, the claims recite that the efficacy enhancing component is either therapeutically active when it is complexed with the therapeutic component or when it is not complexed with the therapeutic component (claims 48 and 49), and that the complex is insoluble (claim 53).

Regarding the rejection of the claims for reciting the term "derivatives", applicant respectfully disagrees with the rejection, but has amended many of the pending claims by removing the term "derivatives" or by making more clear what derivatives are being claimed. Applicant also does not agree with the Examiner's characterization of the term "derivative" as submitted in the previous response. As stated at page 8 of the response, derivatives are defined as any substituted or otherwise modified material that has the characteristic chemical structure of the material recited in a claim to sufficiently function as the recited material. Accordingly, "derivatives" as used in the context of the instant application is not limited to cyclodextrin derivatives, as indicated in the Office Action. For example, quinoxaline derivatives are chemicals that have been modified from quinoxaline but still function like quinoxaline. Applicant respectfully submits that there is no ambiguity with reference to

the term derivatives, and thus the rejections should be withdrawn, particularly with respect to the claims in which the term derivatives have been deleted or more clearly defined.

Regarding the rejection of claims 36 and 60 as allegedly confusing, applicant has amended claims 36 and 60 to make more clear the subject matter for which patent protection is sought.

In view of the above, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Items 3-7 of the Office Action - Rejection Under 35 U.S.C. § 102

Claims 36-39, 41-44, 46-48, and 59-62 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hanssler et al.; claims 36, 37, 41-44, 46-48, 60 and 64 have been rejected as allegedly anticipated by FR 2272684 or JP 62048618. The rejection appears to be based on the Examiner's opinion that a complex inherently forms in the compositions taught by the cited references. Applicant traverses this rejection.

Although the Examiner has taken the position that components of the compositions of the cited references inherently form complexes, the Examiner has failed to provide any evidence that supports that position. Without any evidence to support the Examiner's position, the rejection cannot be maintained.

When a reference is used to anticipate a claim and the reference is silent about the asserted inherent characteristic, extrinsic evidence may be used to fill that gap. "Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference ..."

*Continental Can Co. USA Inc. v. Monsanto Co.* 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749-50 (Fed. Cir. 1991)(emphasis added). "Inherency may not be established by probabilities or possibilities." *Scaltech Inc. v. Retec/Tetra L.L.C.* 178 F.3d 1378, 1384, 51 USPQ2d 1055, 1059 (Fed. Cir. 1999)(emphasis added).

Without any evidence to the contrary, applicant submits that nothing within the cited references, or other art of which applicant is aware, makes clear that complexes necessarily form between the components of the compositions disclosed in the cited references. Therefore, because no evidence has been presented that complexes necessarily form in the compositions of the cited references, the claims are not inherently disclosed by the cited references.

In view of the above, applicant submits that the present claims 36-39, 41, 43-44, 46-48, and 59-62 are not anticipated by Hanssler under 35 U.S.C. § 102(b); and that claims 36, 37, 41, 43-44, 46-48, 60, and 64 are not anticipated by FR 2272684 or JP 62048618.

Item 7 of the Office Action - Double Patenting

Claims 36-68 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of copending application serial number 09/848,249.

As indicated hereinabove, applicant is prepared to submit a terminal disclaimer to address the double patenting rejection. Applicant plans to submit a terminal disclaimer after the other pending rejections are resolved.

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present compositions including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant has shown that the present specification is in proper form, that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 36-41, and 43-68 are allowable. Therefore, applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: SEPTEMBER 16, 2002

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I hereby certify that this correspondence is being transmitted via facsimile to the Commissioner for Patents in Washington, DC 20231, to fax number 703-305-3592 (GAU 1615), on or before: SEPTEMBER 16, 2002

Andrea Uxa

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Abstract:**

The title of the Abstract has been amended as follows:

COMPOSITIONS HAVING ENHANCED PHARMACOKINETIC CHARACTERISTICS [PERMEABILITY THROUGH LIPID MEMBRANES]

**In the Claims:**

Claim 42 has been canceled.

Claims 36, 40, 41, 43-46, 48, 49, 51-53, 59, 60, 63, and 64 have been amended as follows:

36. (Amended) A composition comprising:

a therapeutic component in a therapeutically effective amount, and

an efficacy enhancing component in an effective amount to enhance the pharmacokinetic disposition of the therapeutic component and to [at least one of (1)] enhance the movement of the therapeutic component across a lipid membrane, [and (2) enhance the movement of the therapeutic component across] or a biological membrane under physiological conditions, the efficacy enhancing component being present in a complex with the therapeutic component and being selected from the group consisting of anionic polymers, fatty acids, [derivatives thereof] and mixtures thereof, the complex remaining substantially intact in an aqueous environment, each of enhanced effects being relative to the effect obtained with the therapeutic component without the efficacy enhancing component.

40. (Amended) A composition of claim 39 wherein the quinoxaline component is selected from the group consisting of quinoxaline, (2-imidozolin-2-ylamino) quinoxaline, 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, and quinoxaline derivatives [thereof and] mixtures thereof.

41. (Amended) A composition of claim 36 wherein the therapeutic component is selected from the group consisting of NMDA antagonists, antibacterials, antihistamines, decongestants, antiinflammatories, antiparasitics, miotics, anticholinergics, adrenergics, antivirals, local anesthetics, antifungals, amoebicidals, trichomonocidals, analgesics, mydriatics, antiglaucoma drugs, carbonic anhydrase inhibitors, ophthalmic diagnostic agents, ophthalmic agents used as adjuvants in surgery, chelating agents, antineoplastics, antihypertensives, muscle relaxants, diagnostics, [derivatives thereof] and mixtures thereof.

43. (Amended) A composition of claim 36 wherein the efficacy enhancing component is selected from the group consisting of saturated fatty acids and unsaturated fatty acids, [derivatives thereof] and mixtures thereof.

44. (Amended) A composition of claim 36 wherein the efficacy enhancing component [is selected from the group consisting of] comprises a fatty acid with more than 12 carbon atoms per molecule[, derivatives thereof and mixtures thereof].

45. (Amended) A composition of claim 36 wherein the efficacy enhancing component comprises a docosahexanoic acid [is selected from the group consisting of a docosahexanoic acids, derivatives thereof and mixtures thereof].

46. (Amended) A composition of claim 36 wherein the efficacy enhancing component comprises a linolenic acid [is selected from the group consisting of a linolenic acid, derivatives thereof and mixtures thereof].

48. (Amended) A composition of claim 36 wherein the efficacy enhancing component is therapeutically active when complexed with the therapeutic component [in the complex has a therapeutic effect].

49. (Amended) A composition of claim 36 wherein the efficacy enhancing component is therapeutically active when the efficacy enhancing component is not complexed with the therapeutic component [has a therapeutic effect without being in the complex with the therapeutic component].

51. (Amended) A composition of claim 36 wherein the efficacy enhancing component comprises a prostanoid [is selected from the group consisting of prostanoids, derivatives thereof and mixtures thereof].

52. (Amended) A composition of claim 36 wherein

the therapeutic component comprises a 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline,

the efficacy enhancing component is selected from the group consisting of docosahexanoic acids, linolenic acids, prostanoids, [derivatives thereof] and mixtures thereof; and

the efficacy enhancing component enhances the movement of the therapeutic component across a biological membrane under physiological conditions.

53. (Amended) A composition of claim 36 wherein the complex is insoluble [not present in a solution].

59. (Amended) A composition comprising:

an adrenergic agonist; and

a fatty acid selected from the group consisting of docosahexanoic acids, linolenic acids, [derivatives thereof] and mixtures thereof,

wherein the adrenergic agonist is present in a complex with the fatty acid, the complex substantially remains intact in an aqueous environment.

60. (Amended) A composition comprising a complex and a carrier component, the complex comprising:

a therapeutic component, and

an efficacy enhancing component,

wherein the efficacy enhancing component is selected from the group consisting of anionic polymers, fatty acids, [derivatives thereof] and mixtures thereof, and is present in an amount effective to [at least one of (1)] enhance the movement of the therapeutic component across a lipid membrane, [and (2) enhance the movement of the therapeutic component across] or a biological membrane under physiological conditions, each of the enhanced effects being relative to the effect obtained with the therapeutic component without the efficacy enhancing component.

63. (Amended) A composition of claim 62 wherein the quinoxaline component is selected from the group consisting of quinoxaline, (2-imidozolin-2-ylamino) quinoxaline, 5-bromo-6- (2-imidozolin-2-ylamino) quinoxaline, quinoxaline derivatives [thereof] and mixtures thereof.

64. (Amended) The composition of claim 60 wherein the therapeutic component is selected from the group consisting of NMDA antagonists, antibacterials, antihistamines, decongestants, antiinflammatories, antiparasitics, miotics, anticholinergics, adrenergics, antivirals, local anesthetics, antifungals, amoebicidals, trichomonocidals, analgesics, mydriatics, antiglaucoma drugs, carbonic anhydrase inhibitors, ophthalmic diagnostic agents, ophthalmic agents used as adjuvants in surgery, chelating agents, antineoplastics, antihypertensives, muscle relaxants, diagnostics, [derivatives thereof] and mixtures thereof.

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DATE: September 16, 2002

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FAX: 703-305-3592

FROM: Frank J. Uxa

RE: Patent Application Serial NO. 09/847,935

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